

REMARKS

Applicants respectfully request the Examiner to reconsider the present application in view of the foregoing amendments to the claims and the following remarks.

Status of the Claims

Upon entry of the present response, claims 1, 3, 4 and 6-8 are currently pending in the present application. The Office Action is final. Claims 1 and 6 have been amended, and claim 5 cancelled, without prejudice or disclaimer of the subject matter contained therein. No new matter has been added by way of the amendments. For instance, claims 1 and 6 have been amended to include textual subject matter taken from claim 5, now cancelled. Thus, no new matter has been added.

Based upon the above considerations, entry of the present Amendment is respectfully requested.

Claim Objections

The Examiner states that claim 6 is objected to due to informalities. Applicants have amended claim 6, without prejudice or disclaimer, to include the article "of" as the Examiner suggested.

Applicants respectfully request reconsideration and withdrawal of the present objections.

Issue Under 35 U.S.C. § 103(a), Obviousness

The following rejections under 35 U.S.C. § 103(a) were cited by the Examiner below.

Claims 1 and 5-8 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Gordon *et al.*, “*Protocol for Resolving Protein Mixtures in Capillary Zone Electrophoresis,*” Analytical Chemistry, vol.63, no. 1, pp. 69-72, (1991) (hereinafter “Gordon”) in view of Haupt *et al.*, U.S. Patent No. 3,901,870 (hereinafter “Haupt”).

The Examiner asserts that Gordon discloses the preparation of a sample comprising proteins of interest in water, and in a control experiment, protein in only water, for electrophoretic protein separations. The Examiner further asserts that although the protein in only water is not the preferred method of Gordon, the art does teach the limitation. The proteins separated from the mixture in Gordon were not heat denatured.

The Examiner admits that Gordon does not teach that the electrophoresis buffer has a pH of 2.0 to 9.0. The Examiner further suggests that since Haupt discloses a method of processing a particular protein, wherein Haupt discloses the use of an electrophoresis buffer with a pH from 8 to 9, it would have been obvious to a skilled artisan to use an electrophoresis buffer from pH 8 to 9 as taught by Haupt with the capillary zone electrophoresis method as taught by Gordon. Applicants respectfully traverse.

Although Applicants do not agree with the Examiner’s assertions, in order to advance prosecution, claims 1 and 6 have been amended, without prejudice or disclaimer of the subject matter contained therein, to incorporate the textual subject matter of 5. Claim 5 has been cancelled, without prejudice or disclaimer of the subject matter contained therein, thus obviating this rejection with regard to claim 5.

Graham v. John Deere, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), has provided the controlling framework for an obviousness analysis. A proper analysis under § 103(a) requires consideration of the four *Graham* factors of: determining the scope and content of the prior art; ascertaining the differences between the prior art and the claims that are at issue; resolving the level of ordinary skill in the pertinent art; and evaluating any evidence of secondary considerations (e.g., commercial success; unexpected results). 383 U.S. at 17, 148 USPQ at 467.

M.P.E.P. § 2143 sets forth the guidelines in determining obviousness. But before the Examiner can utilize these guidelines, the Examiner has to take into account the factual inquiries set forth in *Graham v. John Deere*; *supra*. To reject a claim based on the above mentioned guidelines, the Examiner must resolve the *Graham* factual inquiries. MPEP §2143.

If the Examiner resolves the *Graham* factual inquiries, then the Examiner has to provide some rationale for determining obviousness, wherein M.P.E.P. § 2143 sets forth the rationales that were established in *KSR Int'l Co. v Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Applicants respectfully submit that the Examiner has not appropriately resolved the *Graham* factors, including the factors of determining the scope and content of the prior art and ascertaining the differences between the prior art and the claims that are at issue. Based on the following, Applicants maintain that the above mentioned *Graham* factors actually reside in Applicant's favor. Additionally, Applicants submit that since the Examiner did not resolve the *Graham* factors, the rationale the Examiner provides for combining the cited references is improper.

Applicants respectfully submit that the present invention is distinct from the cited references and that the Examiner is basing the Examiner's assertions on hindsight reconstruction.

Differences between the invention and the prior art

As previously indicated, it is described within Gordon that the separation of protein mixtures by capillary zone electrophoresis (CZE) can be plagued by wall adsorption of the protein components. This is not trivial observation or as the Examiner comments, a non-preferred embodiment. Peak broadening and distortion within CZE due to protein adsorption to the walls of the capillary has been a problem in this separation science for years. Gordon reportedly resolves this problem by presenting a method for overcoming wall adsorption of the protein components by adding ethylene glycol to the protein sample (see Gordon, page 69, abstract). More specifically, Gordon describes that the “the sample was prepared by mixing together the following three components in the ratio 1:3:1, namely, proteins of interest in water, 20mM boric acid (pH 4.0), and ethylene glycol” (see Gordon, page 70-CZE Run Conditions). That is, in addition to water, boric acid and ethylene glycol are contained in a sample of Gordon.

Applicants further submit that the Examiner’s rejection is contrary to accepted wisdom, which is evidence of nonobviousness/patentability of what is instantly claimed. *See In re Hedges*, 783 F.2d 1038, 228 USPQ 685 (Fed. Cir. 1986); M.P.E.P. § 2145(X)(D)(3); *see also United States v. Adams*, 383 U.S. 39, 52, 148 USPQ 479, 484 (1966) (“[k]nown disadvantages in old devices which would naturally discourage search for new inventions may be taken into account in determining obviousness.”). Here, at the time the present application was filed, the state of the art was such that it was very difficult in the art to avoid sample adsorption on to the walls of a capillary, thus affecting separation and run times within CZE. Therefore, the present invention has achieved results in an unexpected manner and go against what is shown in the art.

In contrast, the present invention as defined by the amended claims, a protein of interest

is dissolved in a solution that does not contain ethylene glycol so that the present invention separation methodology is unexpected in view of Gordon's comments that the experiments without ethylene glycol resulted in non-reproducible electropherograms.

The Examiner indicates that Haupt is used for its teaching of an electrophoretic buffer with a pH of 8 to 9.

With regard to Haupt, Haupt discusses 1975 electrophoretic technology, and it appears that Haupt describes a conventional zonal electrophoretic method which uses electrophoresis equipment (e.g., a gel plate) that has the dimensions 80 cm x 45 cm and uses polyvinyl chloride as the carrier material in electrophoretic runs in excess of 14 hours.

Haupt discloses at column 5, lines 60-67, that a stiff paste is prepared by mixing a dialyzed protein solution with a dry polyvinyl chloride powder, to yield a stiff paste which was introduced into the electrophoretic apparatus. This mixture is added to a conventional preparative zone electrophoresis, which Applicants respectfully submit is quite different from the present invention. Based on the teaching of Gordon and Haupt as a whole, Applicants also submit that the combination the Examiner provides is inoperable.

In this regard, a claimed combination cannot change the principle of operation of the primary reference or render a reference inoperable for its intended purpose. (See, M.P.E.P. §§ 2143.01, sections entitled "The Proposed Modification Cannot Render the Prior Art Unsatisfactory For Its Intended Purpose" and "The Proposed Modification Cannot Change the Principle of Operation of a Reference," and M.P.E.P. § 2145(III)). The Federal Circuit has also held: "If references taken in combination would produce a 'seemingly inoperative device,' we have held that such references teach away from the combination and thus cannot serve as

predicates for a *prima facie* case of obviousness.” (*See, McGinley v. Franklin Sports Inc.*, 60 U.S.P.Q.2d 1001, 1010 (CAFC 2001), citing *In re Sponnoble*, 405 F.2d 578, 587, 160 U.S.P.Q. 237, 244 (CCPA 1969), holding that references teach away from combination if combination produces seemingly inoperative device; and *In re Gordon*, 733 F.2d 900, 902, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984), finding that an inoperable modification teaches away). Here, the Examiner’s combination does render the Gordon reference as inoperable or destroys its intended function (e.g., separation and resolution of proteins in a quick electrophoretic run in the presence of ethylene glycol) are destroyed with the use of a stiff paste that is somehow introduced into a CZE capillary or having long extended run times for proper separations (i.e., how Gordon would be modified by Haupt) in an attempt to achieve what is instantly claimed.

Thus, one of skill in the art looking to solve the problems disclosed by the prior art references would not modify the references as suggested by the Examiner since this would destroy the teachings of the references. Where the Examiner’s proposed modification would render the prior art version unsatisfactory for its intended purpose, the proposed combination is improper. *In re Gordon*, 733 F.2d 980, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984); see also Ex parte Rosenfeld, 130 USPQ 113 (POBA 1961)

Applicants respectfully submit that it is unlikely that the present invention described above can be derived, suggested or motivated from the teachings of Gordon and/or Haupt.

Applicants also respectfully submit that the present invention is not obvious in light of Gordon and/or Haupt and that the Examiner is applying hindsight reconstruction. While patents or references are relevant as prior art for all they contain, they cannot be relied upon to teach embodiments that are not reasonably suggested to one having ordinary skill in the art. *See Merck*

& Co. v. Biocraft Laboratories, 874 F.2d 804 (Fed. Cir. 1989). In this regard, such hypothetical embodiments are being generated here to achieve the present invention when the Examiner is taking only pieces of each reference and disregarding other essential disclosures of the references. Thus, the cited references are relevant as prior art for all they contain but at the same time cannot be relied upon to teach embodiments that are not reasonably suggested to one having ordinary skill in the art. *See Merck & Co.; supra.*

Accordingly, the Examiner must dissect pieces from the Haupt reference, directed to solving the pH buffer issue, and is combining this piece together with Gordon in an attempt to create a combination and method similar to that defined by the claims of the present application. Thus, through a process of impermissible hindsight reconstruction, the Examiner is completely reconstructing the teachings of the references in view of the Applicants' own disclosure. (*See, Grain Processing Corp. v. American Maize-Products Co.*, 840 F.2d 902, 907, 5 U.S.P.Q.2d 1788, 1792 (Fed. Cir. 1988), stating "Care must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit,'" internal citation omitted; and *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596, 1600 (Fed. Cir. 1988), stating "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."). The Examiner provides Haupt for only the selected teaching of a pH buffer, but does not provide Haupts other teachings (e.g., the addition of the stiff paste, the addition of polyvinyl chloride, or addressing long electrophoretic separation runs) or an explanation of how the above teaching can create a similar method of the present invention.

Thus, through a process of hindsight reconstruction using the Appellants' disclosure (*i.e.*, claims 1 and 6-8), which has been often rebuked by the Courts, the Examiner is improperly modifying and reconstructing the disclosures of the references to a point that they are taken entirely out of context to achieve the methods of the presently claimed invention. (*See, Grain Processing Corp. v. American Maize-Products Co.*, 840 F.2d 902, 907, 5 U.S.P.Q.2d 1788, 1792 (Fed. Cir. 1988), stating, "Care must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit,'" (internal citation omitted); and *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596, 1600 (Fed. Cir. 1988), stating "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.").

In light of the above presently amended claims and remarks, because there is no disclosure, teaching, suggestion, reason or rationale provided in Gordon that would allow one of ordinary skill in the art to arrive at the instant invention as claimed, it follows that the same references are incapable of rendering the instant invention obvious under the provisions of 35 USC § 103(a). Based upon the above, and applying the *Graham factors* analysis test, it is submitted that a *prima facie* case of obviousness has not been established.

Since the present invention is not obvious in light of Gordon, the combinations of Gordon and Haupt also fail. Based on the above remarks, the secondary reference, Haupt, does not cure the deficiencies of Gordon. Therefore, the combinations of Gordon and Haupt do not arrive at the present invention. Based upon the above, and applying the *Graham factors* analysis test, it is submitted that a *prima facie* case of obviousness has not been established for any of the above

mentioned claims. Applicants respectfully request reconsideration and subsequent withdrawal of the above rejection.

Claims 3 and 4 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Gordon in view of Haupt, and further in view Tadayoni-Rebek *et al.*, U.S. Patent Application Publication No. 2002/0155455 (hereinafter Application “‘455”).

The Examiner asserts that Gordon discloses the limitations recited in claim 1 as outlined in the previously discussed 35 U.S.C. § 103(a) rejection. The Examiner admits that Gordon and Haupt do not disclose molecular weight markers subject to electrophoresis together with a protein, as recited in claims 3 and 4.

Further, the Examiner asserts that Application ‘455 discloses high homogeneous molecular markers for electrophoresis, teaches marker molecules comprising a collection of two or more marker molecules, and teaches the addition of the marker molecule composition to a sample containing protein.

Additionally, the Examiner asserts that at the time of the present invention, it would have been obvious to one of ordinary skill in the art to modify the Gordon protocol with the utilization of molecular weight markers taught by Application ‘455 because doing so allows one to obtain highly homogeneous visible molecular markers that are compatible with commercially available separation techniques. Applicants respectfully traverse.

Although Applicants do not agree with the Examiner’s assertions, in order to advance prosecution, claims 1 and 6 have been amended, without prejudice or disclaimer of the subject matter contained therein, to incorporate the textual subject matter of 5, now cancelled.

Applicants respectfully submit that the presently claimed invention is distinct from and

unobvious over Gordon in view of the above cited references. Applicants herein incorporate the previous rejection arguments by reference.

Application '455 fails to compensate for or teach the deficiencies in Gordon or Haupt. As such, for the reasons discussed above, the instant invention of claims 3 and 4 is not obvious over Gordon in combination with Haupt and Application '455; withdrawal of the rejection is respectfully requested.

As discussed above, the secondary references cited above do not cure the deficiencies of Gordon. Therefore, the combinations of Gordon with Haupt and Application '455 do not arrive at the present invention. Based upon the above, and applying the *Graham factors* analysis test, it is submitted that a *prima facie* case of obviousness has not been established for claims 3 and 4. Applicants respectfully request reconsideration and subsequent withdrawal of the above rejections.

In view of the above remarks, Applicants believe the pending application is in condition for allowance.

CONCLUSION

A full and complete response has been made to all issues as cited in the Office Action. Applicants have taken substantial steps in efforts to advance prosecution of the present application. Thus, Applicants respectfully request that a timely Notice of Allowance issue for the present case.

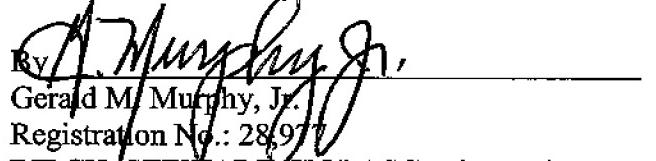
In view of the above remarks, it is believed that claims are allowable.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Paul D. Pyla, Reg. No. 59,228, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

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